REMARKS

Applicant thanks the Office for the attention accorded the present Application in the September 30, 2003, Office Action. In that Action, Claims 1-10 and 17 were rejected under 35 USC §103(a) as being unpatentable over Pearle, Carruthers et al., Abby et al., Oakley et al., and Behounek et al. in view of Rork et al., and Claim 18 was allowed.

The Office admits that the references Pearle, Carruthers et al., Abby et al., Oakley et al., and Behounek et al. do not expressly teach the incorporation of beta-blockers such as timolol, metoprolol, atenolol, and propranolol, and HMG-CoA reductase inhibitors such as pravastatin, folic acid, vitamin B6, and vitamin B12 into a single dosage unit.

The Office cites Rork et al. for the proposition that Rork et al. teaches a sustained release system that can include beta-blockers such as timolol, metoprolol, atenolol, and propranolol and statin cholesterol lowering agents such as simvastatin, pravastatin, and lovastatin. The Office then concludes that it would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate beta-blockers such as timolol, metoprolol, atenolol, and propranolol with HMG-CoA reductase inhibitors such as pravastatin, folic acid, vitamin B6, and vitamin B12 into a single once-a-day dosage unit.

The Office relies on Rork et al. and the knowledge of one of ordinary skill in the art to establish a prima facie case of obviousness, and then responds to Applicants'

previous arguments by stating that the arguments are not found persuasive.

The Office's reliance on *In re Kerkhoven* is incorrect because the Office takes *In re Kerkhoven's* s narrow findings regarding two chemical compositions that each promotes the formation of a nodular structure in cast iron and then generalizes the narrow finding to a broader one. The "very same purpose" in *In re Kerkhoven* is promoting the formation of a nodular structure. The Office discounts the fact that the purpose of each component in Applicants' claimed invention is different and states that Applicants' combination is for the same "thing" (not purpose), i.e. cardioprotection.

This generalization is an overbroadening of the ruling in *In re Kerkhoven*. This is akin to the Office saying, for example, that if one chemical composition in *In re Kerkhoven* had the stated purpose of promoting the formation of a nodular structure in cast iron and the other chemical composition increased the malleability of cast iron (which has nothing to do with the nodular structure formation), both chemical compositions would be useful for the very same purpose, i.e. the ruling of *In re Kerkhoven*. This is clearly incorrect since the purposes in this scenario are different and are an impermissible expansion of the *In re Kerkhoven* ruling. Yet, the Office insists that Applicants' "chemical compositions" have the same purpose when Applicants have shown that beta-blockers block nerve impulses to special sites for the purpose of reducing the rate of heartbeats and the force of heart contractions (this would be equivalent to increased malleability of cast iron) while the lipid-lowering agents "demote" the formation of structure (arterial plaque) along the walls of the arteries (this

would be equivalent to the promotion of nodule formation in cast iron). It is clear that when *In re Kerkhoven* is viewed in proper context, Applicants' components are not used for the **very same purpose**. The Office's conclusion based on the ruling in *In re Kerkhoven* is incorrect because the premises are incorrect.

The Office further misinterprets the Declaration of Dr. Gerry Gurwitz. The Office somehow takes paragraphs 7-9 in Dr. Gurwitz's Declaration to mean that the statements deal only with long-felt need. The Office is clearly wrong. Dr. Gurtz's Declaration states

> "7. Individuals with cardiovascular disorders are known to commonly utilize many medications. Older individuals are in the typical age group in which these cardio-preventative medications are required. Older patients are more susceptible to confusing their multiple medications and multiple treatment regimens.
>
> 8. Despite the industry's many years of knowledge of the benefits of using beta-blockers, of using platelet inhibitors such as aspirin and of using lipid-lowering agents in patients with established cardiac disease, and of the knowledge of compliance problems related to long-term treatments with multiple medications especially in older patients, the general approach is to educate physicians and patients.
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> 9. **Despite my intimate knowledge of adverse drug events, drug prescribing and utilization patterns, and clinical decision-making in the elderly patient population and despite the appreciably higher mortality rates associated with a recurrent acute myocardial infarction than that associated with a first acute myocardial infarction in the United States a h year, I have not**

> **considered and never personally considered, nor has it ever occurred to me to combine beta-blockers and lipid-lowering agents into a single dosage unit as described in the above-captioned application.**" (emphasis added) (Declaration of Dr. Gurwitz, paragraphs 7-9).

Dr. Gurwitz's Declaration is provided as evidence that one of ordinary skill in the art does not find the combination obvious. Dr. Gurwitz's declaration is relied upon as evidence of the knowledge possessed by not only one of ordinary skill in the art but also by the knowledge possessed by one having a higher level of knowledge than one of ordinary skill in the art (specialist in treating the elderly where noncompliance especially with multiple medications is a problem). Dr. Gurwitz's Declaration is also relied upon to support the persuasiveness of Dr. Dean's declaration. Both previously submitted Declarations are also evidence in support of the conventional thinking of ordinary skill in the art relative to the use of beta-blockers and lipid-lowering agents in a single formulation. For years, those of ordinary skill in the art have known of the problems with compliance and under-utilization of beta-blockers and lipid-lowering agents. Yet, even with knowing these problems and knowing the benefits of using beta-blockers and lipid-lowering agents, those of ordinary skill in the art still never suggested the solution embodied in Applicants' claimed invention. The suggestions by those of ordinary skill in the art is now and has always been even at the time of Applicants' invention to educate physicians and patients, not to providing novel means for achieving better patient compliance and utilization results.

In the Office's attempt to circumvent its burden of showing some suggestion, or teaching, or motivation in the cited art that would have motivated one of ordinary skill in the art to combine the medications of Applicants' claimed invention into a single dosage unit, the Office tries to convolute the burdens of proof. In the face of Applicants overwhelming evidence of nonobvious, the Office states that there is (1) no demonstrated evidence of improving compliance, (2) no showing that others of ordinary skill in the art were working on the problem and if so for how long, and (3) no evidence that if persons skilled in the art who were presumably working on the problem knew of the teachings of the above cited references, they would still be unable to solve the problem. The Office has this all wrong.

First, the Applicants are not required to demonstrate evidence of improving compliance. The Office is confusing utility with obviousness. Reduction to practice does not require actual use but only a reasonable showing that the invention will work to overcome the problem it addresses. *Scott v. Finney*, 34 F.3d 1058, 32 USPQ2d 115 (Fed. Cir. 1994). Applicant has provided the reasonable showing throughout Applicants' disclosure. It is the Office that has the initial burden of showing that one of ordinary skill in the art would reasonably doubt the asserted utility, not just concluding that it may.

Second, the Applicants are not required to show that others of ordinary skill in the art were working on the problem and if so for how long. Applicants have the burden of showing that Applicants' claimed invention was nonobvious only after the Office

meets its initial burden of a prima facie case. Again, Applicants disclosure discusses the problems in the prior art and how the problems were addressed by the prior art. Further, Applicants have submitted numerous exhibits that show how those of ordinary skill in the art attempted to solve the problems at the time and that this has not changed even to the present day. Those of ordinary skill in the art relied upon and continue to rely upon their conceived solution to educate physicians and patients on the importance of compliance and the advantages of the two different therapies, i.e. beta-blockers and lipid-lowering agents.

Third, the Applicants are not required to show evidence that if persons skilled in the art who were presumably working on the problem knew of the teachings of the above cited references, they would still be unable to solve the problem. It is the Office's burden to show some suggestion, or teaching, or motivation in the cited art that would have motivated one of ordinary skill in the art to combine the medications of Applicants' claimed invention into a single dosage unit to solve the problems presented. Further, this reasoning by the Office is another way of saying that it would be obvious to one of ordinary skill in the art to try solving the problem in the way disclosed and claimed by Applicants. Obvious to try is not the standard.

The Office maintains its reliance on Rork et al. to teach the use of beta-blockers and lipid-lowering agents. Applicants disagree and submit Applicants' prior arguments as evidence that Rork et al. teach the use of beta-blockers or lipid-lowering agents or any one of the active agents in the long list provided in the Rork disclosure. Rork

contains no teaching, suggestion, motivation, or scientific data to use the device for other than a single drug agent. It is the Office's use of hindsight that provides the link to support the obviousness rejection. Applicants have provided evidence in the form of numerous publications and two Declarations that support a finding of nonobviousness. Despite Applicants' evidence, the Office relies on its own conclusion (not further evidence of a teaching or suggestion or motivation in the cited prior art to counter Applicants' evidence) to maintain its obviousness rejection.

Conclusion

It is clear that when Applicants' invention is viewed as a whole the prior art contains no suggestion to combine Applicants' cardiovascular treatment medications into a single dosage unit. Where Applicants' components are similar to those components shown and disclosed in the prior art, the law requires that the prior art also contain some teaching, suggestion or incentive for arriving at Applicants' claimed structure. The Office has failed to provide this showing. On the other hand, Applicants have provided evidence of noncompliance problems, the under-utilization of medications and the Declarations of Dr. Gurwitz and Dr. Dean (previously submitted) as to the healthcare industries' struggles to find answers to these perplexing questions.

In light of the above arguments, Applicants respectfully submit that Claims 1-10 and 17 of the present application contain allowable subject matter and that the 35 USC §103(a) rejections have been successfully traversed.

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Amendt. Dated March 30, 2004
Reply to Office Action dated September 30, 2003

Applicants believe that all of the pending claims should now be in condition for allowance. Early and favorable action is respectfully requested.

The Examiner is invited to telephone the undersigned, Applicant's attorney of record, to facilitate advancement of the present application.

Respectfully submitted,

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